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EDGE ARTICLE

A dicationic calix[4]pyrrole derivative and its use for the selective recognition and displacement-based sensing of pyrophosphate†‡

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A new bis-pyridinium calix[4]pyrrole derivative is reported. This system forms a non-fluorescent complex upon exposure to the chromenolate anion. The resulting supramolecular ensemble binds the pyrophosphate anion with high affinity ($K_a = (2.55 \pm 0.12) \times 10^7$ M^{-1}) in acetonitrile. It exhibits sensitive "turn-on" fluorescence when exposed to tetrabutylammonium pyrophosphate, and does so in preference to other anions, including the fluoride and phosphate anions.

Introduction

The recognition and sensing of anionic analytes has emerged as an important objective in the supramolecular community due to the ubiquity and importance of anions in a wide range of chemical and biological processes.[1] Among anions of current interest, the pyrophosphate anion has attracted particular attention due to the role it plays in biology, including cellular ATP hydrolysis, real-time DNA sequencing, energy storage, signal transduction and a variety of enzymatic reactions.[2] Moreover, the pyrophosphate anion is a critical marker for DNA replication, which makes it of particular relevance to cancer research.[3]

Not surprisingly, therefore, several synthetic receptors possessing neutral or cationic CH and NH hydrogen bond donor motifs (*e.g.*, triazole, pyrrole, indole, imidazolium, triazolium, ammonium and guanidinium) have been developed in order to achieve selective recognition and sensing.[4] While considerable progress has been made, there still remains a need for receptors that display high selectivity relative to other common anions, including hydrogen phosphate and fluoride anions, which often bind to synthetic anion receptors with high affinity. It would be particularly desirable to have systems that not only display selectivity over fluoride and phosphate (and other anionic analytes), but which also signal the presence of the pyrophosphate anion through a "turn-on" or an easy-to-monitor enhancement in fluorescence intensity, since such detection modes are expected to translate into greater sensitivity and increased ease of use.[5]

While good progress has been made to realizing this goal using metal-based approaches,[4a] potential problems associated with speciation provide an incentive to develop all-organic approaches that address the generalized need for the selective and effective recognition and sensing of pyrophosphate in polar media. Here we report a new design strategy (Scheme 1), based on the functionalized calix[4]pyrrole platform **1**.

Results and discussion

This dicationic receptor bears diametrical bis-(4-methylpyridinium) groups and a cavity that was expected to be ideally suited for the complexation of the pyrophosphate anion *via* a combination of electrostatic interactions and hydrogen bonds. This system was also expected to form a complex with the chromenolate anion, $\mathbf{2}^-$.

This duality in recognition capability, in turn, was expected to allow for the fluorescent "turn-on" sensing of the pyrophosphate anion, in analogy to what has been achieved recently for the fluoride anion using a different modified calix[4]pyrrole system.[6] These expectations were in fact realized. Thus, as discussed further below, receptor **1** in combination with $\mathbf{2}^-$, provides a non-fluorescent complex that allows for the effective, "turn-on" fluorescence-based sensing of the pyrophosphate anion with nanomolar limits of detection in both organic and mixed aqueous organic media. Moreover, good selectivity over the fluoride and phosphate anions was observed.

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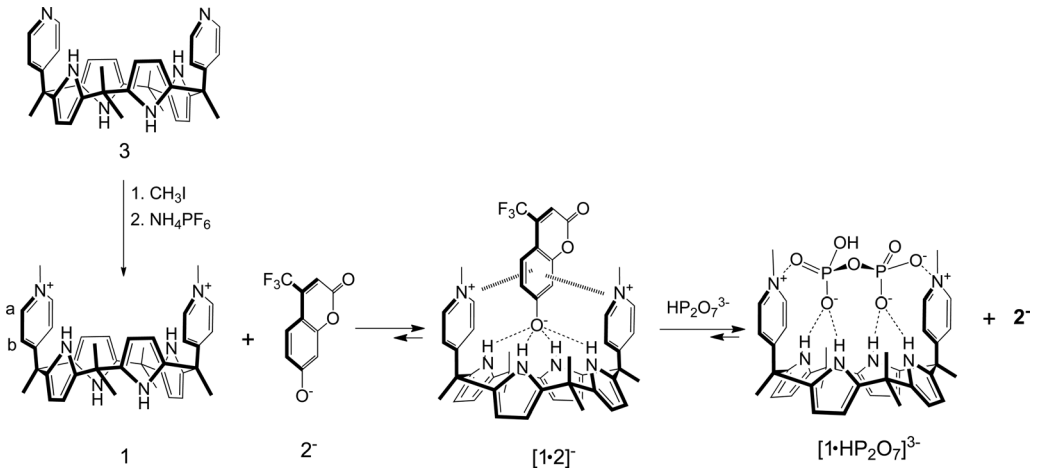
‡ X-ray summary for $\mathbf{1}\cdot\mathbf{2I}^-$: Crystals grew as clusters of yellow laths by slow evaporation from acetonitrile and diethyl ether. The data were collected on a Rigaku AFC12 diffractometer with a Saturn 724 + CCD using a graphite monochromator with MoKa radiation ($\lambda = 0.71073$ Å). Crystal system: monoclinic; space group: $P21/c$; unit cell dimensions: $a = 9.2490(8)$ Å, $\alpha = 90°$, $b = 36.150(2)$ Å, $\beta = 109.970(3)°$, $c = 14.6590(14)$ Å, $\gamma = 90°$. Volume: 4606.5(6) Å^3. Final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0977$, w$R_2 = 0.2019$; R indices (all data); $R_1 = 0.1257$, w$R_2 = 0.2116$; Largest diff. peak and hole: 1.458 and −2.842 eÅ^{-3}. Further details of the crystal structure are found in the Electronic Supporting Information and may be obtained from the Cambridge Crystallographic Data Centre by quoting CCDC number 863400.



Scheme 1 Synthesis of the receptor **1**. Also shown is the proposed FDDA (Fluorescent Dye Displacement Assay) detection of the pyrophosphate anion. As detailed in the text proper, the receptor-bound chromenolate anion $\mathbf{2}^{-}$ is replaced readily by the pyrophosphate anion; this gives rise to an increase in the observed fluorescence intensity. Unless otherwise indicated, all anions were used as their respective tetrabutylammonium salts. The structure of the final complex, $\mathbf{[1\cdot HP_2O_7]^{3-}}$, is inferred from spectroscopic studies. Note: receptor **1** in the absence of the hexafluorophosphate counter anions bears a 2+ charge. However, since the nature and number of the counter ions is not known in the case of the pyrophosphate complex, a designation of −3 for the overall charge has been chosen to emphasize that the $HP_2O_7^{3-}$ anion has been bound. The actual overall charge is likely to be much lower.

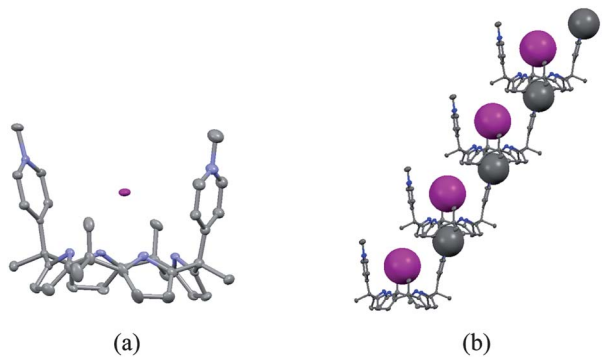


Fig. 1 The single crystal X-ray diffraction structure of the *bis*-iodide complex of receptor **1** (a) and the partial 3D-packing structure (b). One of the iodide anions is not proximate to the receptor and has been removed for clarity, as have the solvent molecules present in the crystal lattice. The thermal displacement ellipsoids in (a) are scaled to the 50% probability level. The carbon atoms are shown in grey, the nitrogen atoms in blue and the iodide ion in purple.

The starting point for our design is the notion that a proper combination of non-covalent interactions will produce systems that display superior analyte sensitivity and selectivity. For the purpose of pyrophosphate recognition, this generalized caveat translated into a need for a receptor that would act as a four-point hydrogen bonding donor (to allow for direct interaction with this linear anion), contains aromatic subunits (to control local solvation and stabilize anion-π interactions), and possess cationic charges (to support coulombic interactions). In addition, the target system should show an inherent fluorescence that could be quenched by the binding of a competitor, thereby allowing for the "turn-on" fluorescence sensing of pyrophosphate *via* an indicator displacement scenario.

The concept of Fluorescence Dye Displacement Assay (FDDA) sensing, which was pioneered by Anslyn and co-workers,[7] has been demonstrated as an effective approach for the

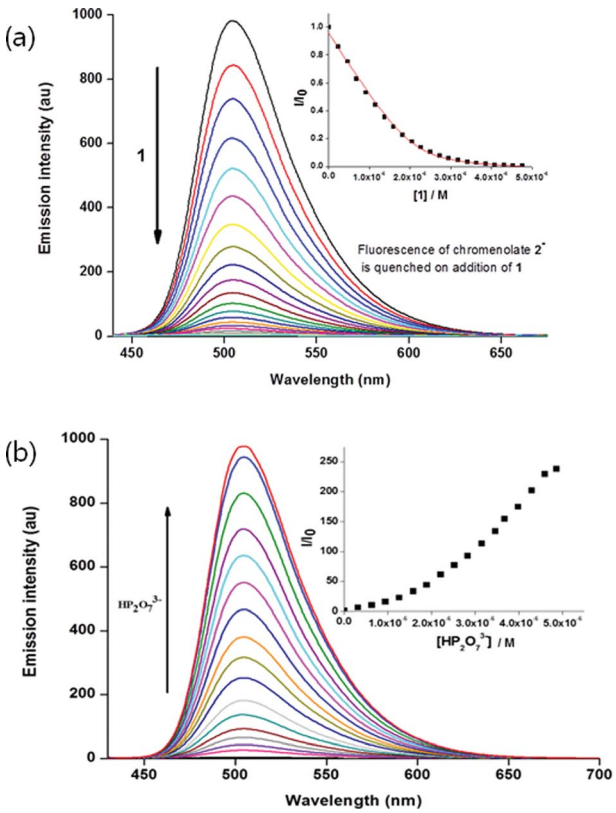


Fig. 2 (a) Changes in fluorescence intensity upon titration of receptor **1** (0–4.8 μM) with the chromenolate anion $\mathbf{2}^{-}$ (2.1 μM) in acetonitrile (λ_{ex} = 410 nm). The inset shows the corresponding Stern–Volmer plot of the associated anion-dependent fluorescence quenching ($K_{SV} = 7.96 \times 10^6$). (b) Recovery of fluorescence of $\mathbf{[1\cdot 2^{-}]}$ upon titration with $HP_2O_7^{3-}$ (as its tetrabutyl ammonium salt, 0–4.9 μM) in acetonitrile at λ_{ex} = 410 nm, **[1]** = 4.8 μM, $[\mathbf{2}^{-}]$ = 2.1 μM; the inset shows a plot of I/I_0 *versus* $[TBA_3HP_2O_7]$.

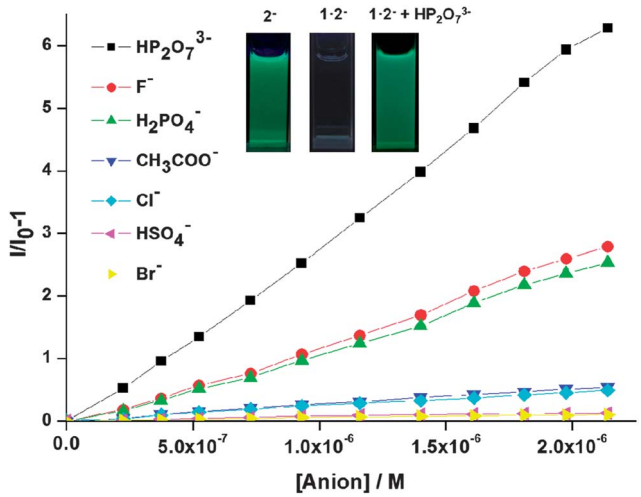


Fig. 3 A comparison of the fluorescence intensity when the preformed complex $[\mathbf{1}\cdot\mathbf{2}]^-$ was treated with various anions (as their tetrabutylammonium salts) in acetonitrile with excitation effected at $\lambda_{ex} = 410$ nm. The experiment was done with the same concentration of receptor, fluorophore and anion ($[\mathbf{1}] = [\mathbf{2}^-] = [\text{Anions}] = 2.1\ \mu M$). The inset shows the observed fluorescence of $\mathbf{2}^-$ (left), $[\mathbf{1}\cdot\mathbf{2}]^-$ (middle) and $[\mathbf{1}\cdot\mathbf{2}]^-$ in the presence of the TBA·$HP_2O_7^{3-}$ (right). Images were obtained with a UV lamp ($\lambda_{ex} = 365$ nm).

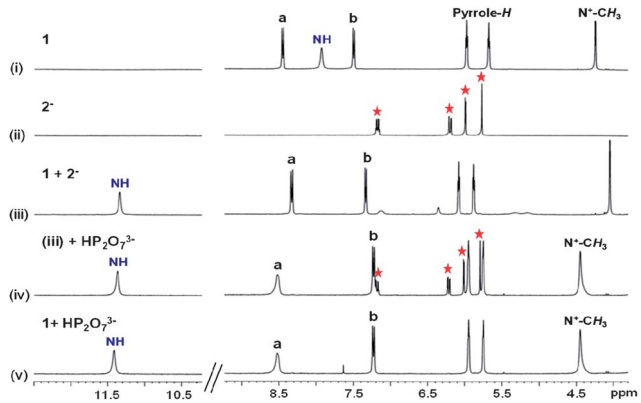
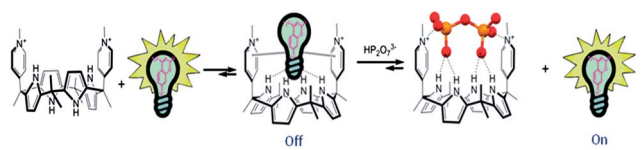


Fig. 4 Partial ^{1}H NMR (300 MHz; acetonitrile-d_3) spectra of various solutions containing (i) **1** only (4.57 mM), (ii) $\mathbf{2}^-$ only (4.66 mM), (iii) **1** + $\mathbf{2}^-$ (1.02 equiv.), (iv) the mixture present in (iii) + $HP_2O_7^{3-}$ (1.45 equiv.) and (v) **1** + $HP_2O_7^{3-}$ (1.45 equiv.). All anions were studied in the form of their corresponding tetrabutylammonium salts.



Scheme 2 A schematic representation of the present FDDA-based approach to pyrophosphate anion detection. See text for details.

selective detection of numerous analytes. Nevertheless, the guest-dependent, fine-tuning of the FDDA approach is a challenging task and progress in this area may benefit from new strategies that permit the selective recognition of analytes with high detection limits. We have now found that combining the

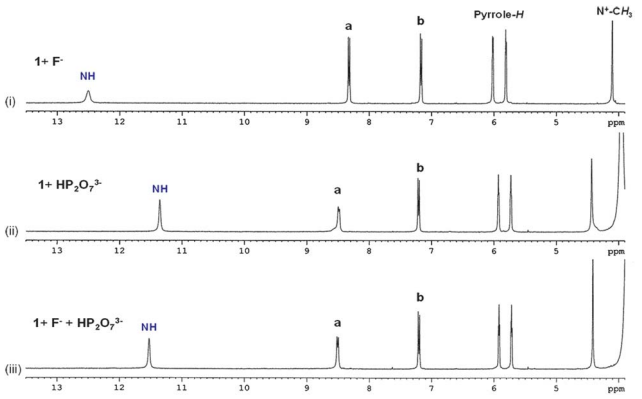


Fig. 5 ^{1}H NMR spectroscopic competition experiments carried out in CD_3CN. (i) **1** + F^- (1.2 equiv.), (ii) **1** + $HP_2O_7^{3-}$ (1.2 equiv.) and (iii) **1** + F^- + $HP_2O_7^{3-}$ (1.2 equiv. each). $[\mathbf{1}] = 4.57$ mM. Both anions were studied in the form of their tetrabutylammonium salts.

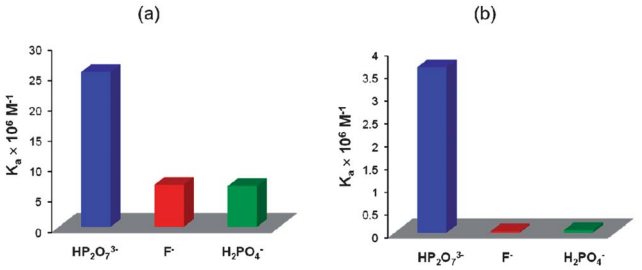


Fig. 6 Bar graphs showing the relative and absolute binding affinities corresponding to the interaction of three test anions with receptor **1** (a) in pure acetonitrile and (b) in 30% water in acetonitrile.

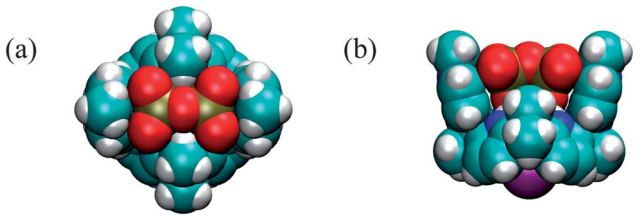


Fig. 7 (a) Top and (b) side view of the most stable structure for the complex $\mathbf{Cs[1\cdot HP_2O_7]^{3-}}$ in a space filling representation.

fluorophore, tetrabutylammonium-2-oxo-4-(trifluoromethyl)-2*H*-chromen-7-olate ($\mathbf{2}^-$),[6] with the newly designed cationic calixpyrrole **1**, allows for the FDDA-type recognition and sensing of the pyrophosphate ($HP_2O_7^{3-}$) anion.

We recently described a neutral calix[4]pyrrole–chromenolate complex and its use as a FDDA for fluoride anion.[6] This supramolecular ensemble exhibited a dramatic and highly selective "turn-on" increase in fluorescence intensity when exposed to the fluoride anion. The mechanism for the "turn-on" increase in the fluorescence intensity involves the near-exclusive displacement of the initially bound fluorophore ($\mathbf{2}^-$) by the fluoride anion. Almost negligible fluorescence changes ($\ll$3.3% of those induced by F^-) were seen in the presence of most of the other anions, including the pyrophosphate anion. In an effort to generalize our original, fluoride-selective FDDA strategy so that

it could be applied to the more challenging problem of pyrophosphate recognition and sensing, we sought to modify the calix[4]pyrrole core. With such considerations in mind, we have now prepared the bis-pyridinium calix[4]pyrrole **1**. This new receptor forms a completely non-fluorescent supramolecular ensemble $[\mathbf{1}\cdot\mathbf{2}]^-$ with the highly fluorescent chromenolate anion $\mathbf{2}^-$. When the non-fluorescent complex, $[\mathbf{1}\cdot\mathbf{2}]^-$ was treated with pyrophosphate anion (as its tetrabutylammonium (TBA) salt) in acetonitrile, a dramatic increase in fluorescence intensity was observed. The underlying optical changes are ascribed to the formation of a pyrophosphate–receptor complex, $[\mathbf{1}\cdot\mathbf{HP_2O_7}]^{3-}$ that is more stable than $[\mathbf{1}\cdot\mathbf{2}]^-$ was as the result of displacing $\mathbf{2}^-$ by the pyrophosphate anion. Due to differences in the extent of displacement, the original complex, $[\mathbf{1}\cdot\mathbf{2}]^-$, is capable of differentiating pyrophosphate over dihydrogen phosphate ($H_2PO_4^-$) as well as the fluoride anion. These differences in degree of displacement, as well as the high selectivity and sensitivity seen for the pyrophosphate anion, are ascribed to the synergistic effects of several non-covalent interactions, including hydrogen bonding, anion-π interactions and multiple electrostatic contacts.

The bis-pyridnium calix[4]pyrrole **1** as its hexafluorophosphate salt was obtained in moderate yield *via* methylation of the corresponding *cis*-5,15-(4-pyridyl)calix[4]pyrrole **4**, a species that, in turn, was prepared by condensing 5-(4-pyridyl)dipyrromethane with acetone (ESI†). Receptor **1** was characterized by standard spectroscopic methods and the structure was further confirmed through a single crystal X-ray diffraction analysis of the di-iodide salt. This structural analysis revealed that one iodide anion is localized within the cavity. In analogy to what is observed for a wide variety of calix[4]pyrrole anion complexes,[8] the bound anion is stabilized through four hydrogen bonds, as inferred from the close N–H···I contacts that range 2.805–2.874 Å. The distance between the two diametrical pyridinium N^+ centers was found to be 8.787 Å, which was considered to be particularly suitable for the recognition of the pyrophosphate anion *via* "end-to-end" interactions, as suggested in Scheme 1.

In addition to confirming the interaction with a bound iodide anion, the above structure revealed that individual calix[4]pyrrole "monomers" self-assemble to produce a polymerized ensemble in the solid state, as inferred from analyses of the packing diagram (*cf.* Fig. 1). This aggregated structure appears to be stabilized through π-cation interactions involving the docking of an *N*-methyl group on one pyridinium moiety into the cup of a neighboring anion-bound receptor. One of the pyridinium groups in **1** is slightly more tilted than the other, presumably as a result of this interaction.

In accordance with what was seen previously in the case of the *meso*-bis(*p*-fluorophenyl)calix[4]pyrrole used for fluoride anion sensing,[6] the incremental addition of receptor **1** to an acetonitrile solution of the highly fluorescent dye, $\mathbf{2}^-$, in acetonitrile resulted in a concentration-dependent decrease in absorbance (followed at 434 nm) and a concomitant quenching of the inherent fluorescence for $\mathbf{2}^-$ (for which λ_{em} is centered at 500 nm; Fig. 2a). Near-complete quenching of the fluorescence (≥99%) was observed, along with a 56 nm hypochromic shift in the absorption maximum in the UV-vis spectrum upon addition of *ca.* 4.76 μM of **1** to an acetonitrile solution containing 2.1 μM of $\mathbf{2}^-$. Most of the quenching is observed by the time one molar equivalent had been added (*cf.* Fig. 2).

These changes are consistent with the formation of the non-fluorescent receptor–chromenolate ensemble $[\mathbf{1}\cdot\mathbf{2}]^-$, with the lack of fluorescence being specifically ascribed to the dissipation of excitation energy through the multiple hydrogen bonds that would be expected within such a complex. A Job plot analysis, obtained from the absorption changes, showed a maximum at a mole fraction of 0.5, as would be expected for a 1 : 1 receptor/anion stoichiometry. Likewise, regression of the data allowed an affinity constant of $K_a = (7.25 \pm 0.12) \times 10^6\ M^{-1}$ to be calculated for $[\mathbf{1}\cdot\mathbf{2}]^-$ in acetonitrile.[9]

The interactions between **1** and $\mathbf{2}^-$ were also analyzed using ^1H NMR spectroscopy. The analyses revealed that successive additions of $\mathbf{2}^-$ to a solution of **1** in CD_3CN resulted in a broadening of the signal corresponding to the protons of $\mathbf{2}^-$; it also produced up-field shifts in the protons *ortho* to the anionic center. Moreover, the pyrrole N–*H* resonances of **1** are shifted down-field, ultimately converging to δ 11.35 ppm. These changes in the spectral features support the notion that **1** interacts with $\mathbf{2}^-$ in a cofacial manner *via* a combination of N–H···O-Ar hydrogen bonding and π–π interactions.[10] The fact that only a stoichiometric amount of $\mathbf{2}^-$ (1.02 equiv.) is required to reach nearly complete saturation is fully consistent with the 1 : 1 binding stoichiometry.

The utility of preformed complex $[\mathbf{1}\cdot\mathbf{2}]^-$ for the FDDA sensing of the pyrophosphate anion was studied by titration of $[\mathbf{1}\cdot\mathbf{2}]^-$ with $HP_2O_7^{3-}$ (as the TBA salt) in acetonitrile. The sequential addition of pyrophosphate anion resulted in the enhancement of the fluorescence intensity depending on the released [$\mathbf{2}^-$]. The original fluorescence of the same concentration of $\mathbf{2}^-$ was fully recovered (*ca.* ~1000-fold enhancement relative to $[\mathbf{1}\cdot\mathbf{2}]^-$) at 4.9 μM of $HP_2O_7^{3-}$ in acetonitrile (Fig. 2). For solutions containing equal quantities of **1** and $\mathbf{2}^-$ (2.1 μM of each, Fig. 2b), the maximum intensity was recovered upon addition of the same concentration of pyrophosphate anion. The "turn-on" fluorescence changes produced by addition of the pyrophosphate anion can also be easily visualized by the use of a simple UV-lamp.

In contrast to what is seen with pyrophosphate, the addition of other anions, such as F^-, $H_2PO_4^-$, $CH_3CO_2^-$ and Cl^- (all studied as their TBA salts), resulted in relatively small enhancements (Fig. 3). Moreover, only negligible changes in fluorescence intensity were observed in the case of either HSO_4^- or Br^-. These results support the contention that this assay is preferentially sensitive towards the $HP_2O_7^{3-}$ compared to other anions.

Furthermore, a measurable fluorescence enhancement was seen even in the presence of very low concentrations of $HP_2O_7^{3-}$ (up to 0–110 nM). On the basis of specific quantitative analyses, a detection limit of ~2 ppb was calculated (ESI†). Such a detection limit represents a dramatic improvement in sensitivity relative to what has been achieved previously using a chemically modified calix[4]pyrrole system.[11]

Further support for the contention that pyrophosphate anion completely displaces the receptor-bound fluorophore from the preformed complex $[\mathbf{1}\cdot\mathbf{2}]^-$ came from ^1H NMR spectroscopic analyses (Fig. 4). Specifically, when 1.45 equiv. of pyrophosphate ($HP_2O_7^{3-}$) were added to a solution of $[\mathbf{1}\cdot\mathbf{2}]^-$ in acetonitrile-d_3 the final spectral patterns matched those of the

complex $[\mathbf{1}\cdot\mathbf{HP_2O_7}]^{3-}$ prepared independently by mixing the TBA salt of pyrophosphate anion with receptor **1**.

Mass spectrometric analysis (MALDI-TOF MS) also provided evidence for the formation of the pyrophosphate complex $[\mathbf{1}\cdot\mathbf{HP_2O_7}]^{3-}$ (ESI†). As shown in Scheme 2, the supramolecular 'On–Off–On' type of fluorescence displacement protocol reported here allows for the sensitive recognition and sensing of $HP_2O_7^{3-}$ over other anions.

Fluorescence dye $\mathbf{2}^-$ forms a strong supramolecular complex with receptor **1**, with concomitant quenching of the fluorescence. The quenching of fluorescence seen upon formation of $[\mathbf{1}\cdot\mathbf{2}]^-$ is ascribed to photo-induced electron transfer (PET) from the calix[4]pyrrole to the excited state of $\mathbf{2}^-$. The high stability of complex $[\mathbf{1}\cdot\mathbf{2}]^-$ is thought to reflect the synergistic effects of π–π interactions involving the chromenolate anion and the electron-deficient pyridinium-functionalized calix[4]pyrrole and multiple hydrogen bonds between the pyrrole N–Hs and the bound chromenolate anion. In the presence of the pyrophosphate anion, however, the bound fluorescence dye $\mathbf{2}^-$ is again completely displaced by pyrophosphate anion. In operational terms, the affinities for anions were found to decrease according to the following sequence: $HP_2O_7^{3-} > F^- \approx H_2PO_4^- \gg CH_3COO^- \approx Cl^- \gg HSO_4^- \approx Br^-$, as calculated from separate fluorescence titration analyses.

In support of this assessment, the affinity constants (K_a) corresponding to the interaction between receptor **1** and the anions in question (as the TBA salts in acetonitrile) were independently determined *via* UV-vis absorption titrations[8] and were found to be well-matched with this selectivity order. The exceptionally high affinity observed for the interaction between receptor **1** and the pyrophosphate anion may reflect a number of factors, including the presence of appropriately spaced cationic charges, a proper dimension for the binding domain, stabilizing anion–π interactions and the presence of multiple hydrogen bonds. Among these factors, the presence of two cationic charges in receptor **1** appears to be essential for the observed sensitivity. Consistent with this assessment is the finding that the association constant for the interaction between the pyrophosphate binding and the neutral bispyridine receptor **4** ($K_a = (5.25 \pm 0.50) \times 10^5\ M^{-1}$) is much smaller than that for the interaction of the pyrophosphate anion and receptor **1** ($K_a = (2.55 \pm 0.12) \times 10^7\ M^{-1}$).

Hydrogen bonds also presumably play a role in regulating the observed pyrophosphate selectivity displayed by receptor **1**. As shown in Scheme 1, two (out of three) of the anionic oxygen atoms present in the pyrophosphate anion form two point hydrogen bonds with the four pyrrole N–Hs. Concurrently, the two pyridinium cations are observed to interact with two of the other anionic oxygen atoms through electrostatic interactions. On this basis, we conclude that the dimensions of the cavity present in **1** match well in terms of size and charge distribution of the pyrophosphate anion. Consistent with this conclusion, ^{1}H NMR spectroscopic studies revealed a significant peak-broadening for the protons *ortho* to the N^+ centers (Fig. 4) in **1**. However, no such broadening was observed in analogous experiments carried out with the dihydrogen phosphate anion (ESI†).

To understand the selectivity of receptor **1** for the pyrophosphate anion over other anions, the rate of deuterium exchange was studied. Upon addition of 2.2 molar equiv. of D_2O to a solution of free receptor **1** in acetonitrile-d_3, the signals for the NH protons disappeared instantaneously due to fast H–D exchange. However, the half-life of the pyrrole N–H signal in the case of complex $[\mathbf{1}\cdot\mathbf{HP_2O_7}]^{3-}$ under these same conditions was over three days. The latter exchange process displayed first order kinetics with the calculated rate constant being $k = 6.0 \times 10^{-4}\ h^{-1}$ (see ESI†). This extremely modest H–D exchange rate is thought to reflect the presence of strong hydrogen bonding interactions between the pyrophosphate anion and the pyrrole N–Hs. Presumably, the additional electrostatic interactions provided by the pyridinium moieties of receptor **1** in the case of $HP_2O_7^{3-}$ make the exchange even slower. Unlike neutral calix[4]pyrrole-based receptors,[6] the cationic receptor **1** can hold the bound pyrophosphate anion strongly, even after addition of excess Na^+ (ESI†). This lack of competition is attributed to the fact that receptor **1** contains positive charges that repel these cations.

The F^- anion is typically bound very well by pyrrolic receptors.[6] Competition experiments with the pyrophosphate anion were thus carried out. Here, an equimolar mixture of TBAF and $(TBA)_3HP_2O_7$ was treated with receptor **1** in CD_3CN, as shown in Fig. 5. The results provide support for the conclusion that receptor **1** forms a complex with the pyrophosphate anion exclusively, and does so even in the presence of the fluoride anion.

Even in the presence of excess H_2O, receptor **1** still forms a stable complex with $HP_2O_7^{3-}$. The binding constant for the receptor **1** with pyrophosphate anion, measured in 30% water ($K_a = (3.63 \pm 0.23) \times 10^6\ M^{-1}$) is roughly ~1/7 of the value measured in pure acetonitrile ($K_a = (2.55 \pm 0.12) \times 10^7\ M^{-1}$). However, the corresponding affinities for F^- and $H_2PO_4^-$ (both as the TBA salts) were found to be dramatically reduced in the presence of water, being *ca.* ~1/276 and ~1/140 lower for fluoride and dihydrogen phosphate, respectively, in 30% aqueous acetonitrile (Fig. 6). On this basis, we suggest that the sensor system reported here becomes more selective towards the pyrophosphate anion as the water content increases. This enhancement in relative selectivity in the presence of water is thought to reflect the high hydration energies of the rather basic anions F^- and $H_2PO_4^-$ as compared to the pyrophosphate anion ($\Delta G^\circ \approx -465$ KJ mol^{-1} for both anions).[12]

Fig. 7 shows the DFT-based optimized structure of the pyrophosphate complex of the receptor **1** and well fit of the anion to the cavity.[13–15] The cooperative actions of the pre-organized binding domain, hydrogen bonding donor and Colombic interaction give exceptionally strong affinity.

The structure reveals that the hydrogen on the pyrophosphate anion reside between the two oxygen which are bound to the pyrrole N–Hs.

Conclusions

We have detailed an efficient fluorescence dye displacement assay that acts as a specific sensor for the pyrophosphate anion in pure acetonitrile. The selectivity for the pyrophosphate anion relative to other tested anions, including F^- and $H_2PO_4^-$, is enhanced even further in the presence of water (*i.e.*, acetonitrile containing 30% H_2O). The preference for the pyrophosphate anion is rationalized in terms of its ability to form a stronger

supramolecular complex with **1** than the other test anions. Presumably, this reflects the combined benefit of several favorable interactions, including electrostatic, anion–π and hydrogen bond interactions. The current work thus provides insights into the basic principles that may be applied to the design and synthesis of analyte-specific receptors. The proper tuning of various weak interactions combined with a "turn-on" approach as provided by displacement may provide a general strategy for the development of fluorescence sensors for a wide range of analytes. Tests of this hypothesis and efforts to generalize the concepts detailed in this report are currently ongoing.

Acknowledgements

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Notes and references

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